March 25, 2008

Richard Keller
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210 King Street
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Re: CIRM RFA 07-03
Application #FA1-00607-1 (CIRM Institute)

Dear Rick:

Thank you for the opportunity to comment on the staff analysis ("Analysis") of the San Diego Consortium for Regenerative Medicine ("SDCRM") Part 2 Major Facilities Application ("Application").

As noted in the Analysis SDCRM is the only consortium formed in response to the Application. We appreciate the staff's recognition that an important "innovation of this proposal is the formation of a consortium that will allow researchers from several institutions to co-locate and collaborate in ways that would not otherwise be possible."

However, we are disappointed that the staff did not include in its Analysis consideration of the full value of the consortium. Four organizations with mature track-records have allied to apply as one, proposing one shared facility, instead of creating as many as four separate facilities. Each of SDCRM's member organizations has substantive complementary research strengths which, combined, create a synergistic research enterprise, the whole of which is substantially greater than the sum of its parts. SDCRM is thus poised to make significant contributions in the development of stem cell-based diagnostics , therapeutics and cures for debilitating conditions and to create the next generation of young scientists, physicians, and biomedical leaders in California.

A $50 million investment in SDCRM's facility (the "Facility") represents an extraordinarily efficient and effective use of Proposition 71 funds. The purpose built Facility will enable the collaborative science required to hasten the pace of progress in stem cell science and medicine by creating functional, flexible and innovative spaces to support SDCRM's basic, translational, and preclinical research programs each of which received the highest scores awarded by the Grants Working Group ("GWG").

The GWG "lauded [SDCRM's] proposed [Basic Research] program as a model for collaboration, and felt that the participants are the who's who of stem cell research…" They "very enthusiastically" supported SDCRM's Translational disease team-oriented research program saying that it represented "an excellent transition from basic research"…and described its translational technology proposal as being "really clever…light years ahead in the way they are thinking about delivery systems for cells." The Group

finally concluded that the SDCRM Preclinical Development program's "proposed studies break away from dogma and aim for a very sophisticated, cutting edge level [of preclinical science]".

To satisfy the functional requirements of its extraordinary science program, diverse expertise and opinions were sought and considerable effort was expended to explore and develop innovative design ideas to ensure that the Facility would satisfy the unique functional demands of SDCRM's multi-institutional as well as multi-disciplinary science program.

The Facility will well serve the needs of SDCRM's extraordinary science. But, it does not fit a traditional model. Thus, application of traditional design benchmarks, without consideration of the unique demands of SDCRM resident and non-resident stem cell scientists can lead to incorrect and unfair conclusions.

The Analysis includes several statements and conclusions that we believe warrant clarification. Our comments herein are directed solely to correct or clarify. We do so by reproducing sections of the Application to reemphasize how aspects of the Facility's design are functionally integral to the fulfillment of SDCRM's top rated science program.

We respectfully request and appreciate your careful consideration of our reply.

Functionality

The Facility is purpose-built. It is located nearly equidistant from each of the SDCRM member organizations amidst the large, thriving and interactive community of research institutes, biotechnology and pharmaceutical companies on Torrey Pines science mesa. It is intended to engage and catalyze the entire Torrey Pines science community to participate in and contribute to the collaborative, interdisciplinary science that is the foundation of a comprehensive CIRM Institute.

All of the space included in the CIRM-funded portion of the Facility was designed and included specifically to support the functional needs of the SDCRM science program…to bring together basic, translational, and preclinical research teams in a space that can enhance and facilitate multi-disciplinary collaboration.

The Analysis correctly acknowledges the abundance of strategically placed informal and formal meeting and education spaces all intended to maximize face-to-face interactions among SDCRM resident and non-resident scientists as an innovation (p.5)

However, the Analysis goes on to *incorrectly* posit that,

> *"The amount of space devoted to building 'amenities' is excessive in comparison with other proposals and results in a higher cost facility than is needed to accommodate the core program need (p.3) [and that] the core mission could be accomplished without incurring the expense for these amenities (p.7)."*

The collaborative spaces that are the subject of the Analysis's concern are not amenities. SDCRM's core mission cannot be accomplished without these spaces.

They are scholarly activity areas, "research neighborhoods", and are the product of the innovative design process that was described in the Application and was intended to create spaces where multi-disciplinary research among biologists, chemists, engineers and physicians and teaching, training and community outreach activities could occur.

In the Application we described the Facility as a stem cell collaboratory[1], in which scientists from four of the nation's leading research institutions will work in focused teams to address critical health issues using cutting edge science and technology. The Facility will serve as the 'hub' of San Diego's extraordinary stem cell research community and its academic and industrial collaborators as the 'spokes'. Its design will encourage the expansion of extant groups and the formation of new *collaborations* between multi-disciplinary scientists.

The strategically placed informal and formal meeting and education spaces are intended to maximize face-to-face interactions among not only the approximately 20 *resident* SDCRM faculty, but also the more than 100 *non-resident* SDCRM faculty members and academic and industrial collaborators thereby to enable the realization of SDCRM's scientific four point vision (1) to stimulate creative approaches to complex medical problems by promoting collaboration, (2) to invent the next generation of tools and instrumentation, (3) to recruit and train the next generation of scientists whose approach to solving medical problems is interdisciplinary and (4) to inform and educate the public about our scientific and medical progress and aspirations.

Non-resident faculty will include outstanding basic and clinical research faculty drawn from member institutions as well as other academic and industrial collaborators. Non-resident Faculty are critical for translation of basic science discoveries in four main ways: the further understanding of fundamental aspects of stem cell biology (including genetics and epigenetics from mammalian and non-mammalian simple systems); development of appropriate models of disease; development of cell transplantation techniques to restore normal function, and testing of experimental therapies in these model systems.

Because Non-Resident Faculty will outnumber Resident Faculty by more than 5:1, and because the diverse talents of Non-Resident Faculty members are so essential to the realization of SDCRM's scientific vision, special attention was made in the Facility's design to include spaces that invite, encourage, and afford Non-Resident Faculty the means to work at the facility. The exterior plaza and interior atriums, the auditorium, cafeteria, and numerous meeting, brainstorming rooms, studies and teaching facilities are integral tools to satisfy the functional needs of not only San Diego's large and diverse stem cell science community but disease research and patient advocacy groups as well.

Research neighborhoods are laboratories without benches and are integral elements of the Facility necessary to satisfy the Facility's principal *functional* purpose… enhance and facilitate collaborative research.

On page 3, The Analysis contends that…

[1] "A networked organizational form that also includes social processes; collaboration techniques; formal and informal communication; and agreement on norms, principles, values, and rules Cogburn, D. L. (2003). HCI in the so-called developing world: what's in it for everyone, *Interactions, 10*(2), 80-87, New York: ACM Press

> *"100% of the cost of the building amenities should not be attributed to leverage, because this space is also available to other building occupants that are not part of the CIRM Institute space."*

We agree. In fact, SDCRM took great care to fairly and accurate allocate space and the corresponding cost between the CIRM funded and non-CIRM funded space.

SDCRM isolated the flexible space to one complete floor in the building. This floor includes its own meeting, office and conference spaces. All of these spaces, and the corresponding cost, were treated as non-CIRM funded space. Of the 32,910 asf Other Office and Administrative Support spaces, 7,580asf or 23% of the space and 23% of the corresponding cost was treated as non-CIRM funded space and was not counted as leverage.

As noted in the Application, SDCRM fully expects that the entire Facility, including the non-CIRM funded space, will be occupied by stem cell researchers when the Facility opens. If not, however, users of the non-funded space would relocate only discrete operations whose space needs could be limited to the designated leased space, until such space is required to accommodate the needs of stem cell scientists. While the CIRM funded space might 'appear attractive to occupants of the space not attributed to CIRM', because these spaces are critical to SDCRM's mission, SDCRM can and will limit access to them.

On page 3, the Analysis states,

> *"For purposes of establishing a fair share of facilities costs attributable to the CIRM proposal, we have evaluated the building cost and space program with the principle that 71% of the space and the costs attributable to the CIRM proposal and 29% of the space and costs are attributable to the flexible space. The applicant, however, has assigned various ancillary support spaces between the two major building programs and allocated building costs using different allocation assumptions."*

As noted above SDCRM took great care to fairly and accurately allocate space and the corresponding cost between CIRM funded space and non-CIRM funded space. For reasons cited above, we do not believe that a 'straight-line' allocation of *all* costs results in a fair and accurate distribution of costs.

The cost of the Facility's *core and shell* costs were allocated in the straight-line manner recommended in the Analysis. The cost of interior improvements however, was allocated considering the amount of each specific space type (laboratory, offices, etc.) assigned to CIRM and non-CIRM space and the specific estimated cost of each. We contend that this allocation method results in a fair allocation of costs between the CIRM funded and the non-CIRM funded space.

Leverage

Land

On page 3, the Analysis concludes that,

> *"Because the applicant is not using any funds to purchase the land or the ground lease, there is no documented cost to the consortium and therefore no basis in the FWG guidelines for including the $14.5 million as part of leverage."*

SDCRM is using funds to purchase right to use the land at a documented cost to SDCRM and so according to the Grants Administration Policy, the cost of land should be included in Total Project Costs and counted as leverage.

SDCRM is an independent non-profit public benefit corporation exempt from taxes under section 501(c)(3) of the Internal Revenue Code and is governed by a fifteen member Board of Directors comprising one member from each of the member organizations and eleven community leaders. SDCRM is not controlled nor can it be significantly influenced by any one of its members.

SDCRM will obtain rights to use the land to develop, occupy and operate the facility via a ground lease with UCSD. The 52 year lease was negotiated at arm's length and on terms similar to other ground leases entered into by UCSD with other independent organizations. SDCRM is obligated to pay rent based on a ten percent (10%) return on the mutually commissioned appraised fair market value of the land, which based on recent, comparable appraisals is $142/buildable square foot. The 'capitalized' lease cost of the CIRM funded share of the Facility is thus $14.4 Million or 101,667 gsf * $142/gsf).

According to Statement of Accounting Standards #13 (SFAS #13), "Accounting for Leases" SDCRM will reflect the lease as an *operating lease* in its financial statements and will be required to disclose in the footnotes to its financial statements future minimum rental payments in the aggregate and for each of the five succeeding years.

To the extent that SDCRM uses all or a portion of the building for approved uses, UCSD has generously offered to grant to SDCRM a credit in proportion to such approved use. SDCRM will account for this rent credit as a 'contribution' as prescribed by SFAS 116 and will record the value of the anticipated credit as a *temporarily restricted* asset at the inception of the lease and will amortize its value and recognize same as unrestricted contribution income annually when realized.

SDCRM will pay a documented cost for the use of the land using funds contributed, albeit retrospectively, by an independent donor, UCSD. Consequently, pursuant to the Grants Administration Policy the documented cost of the land should be included in Total Project Costs and counted as leverage***.***

Parking
On Page 3 the Analysis contends that,

> *"The cost of parking improvements is an ancillary cost that all other applicants have addressed outside of the grant proposal. [Parking] is a service (like utilities) that is to be provided by the institution to support the needs of the users of the facility."*

Irrespective of the treatment of such costs by other applicants, (who likely can rely on existing infrastructure) provision of parking is required to make the building operational. The expenditures for parking improvements qualify to be capitalized consistent with the usual practices of the University of California and thus are properly included in Total Project Costs.

The FAQ for RFA 07-03 advise that Total Project Costs includes all costs that qualify to be capitalized consistent with the usual practices of the University of California.

The UCOP Accounting manual P 415-1, Capitalization of Property, Plant and Equipment requires, consistent with Generally Accepted Accounting Principles (GAAP), the capitalization of costs associated with the acquisition or construction of property, plant and equipment. For Construction projects the Manual provides that all direct construction costs should be capitalized.

Excess space
On page 3, the Analysis concludes that

> *"Our review of the plans indicates that 10,200 gsf of common space would be more properly assigned to the non-SDCRM project costs based on the amount of laboratory space reserved for CIRM and ratio of CIRM funded space to the non-CIRM funded space. Using a very conservative value of $250/gsf for this space there is an additional $2.5 million in costs that should not be counted as leverage and should be assigned to funding separate from the CIRM funded project."*

In addition to the reasons cited above, because the proposed adjustment does not consider the amount of space, and the corresponding cost that SDCRM did allocate to the non-CIRM funded space, we believe that the $2.5 million adjustment is unwarranted.

As noted previously, SDCRM took great care to fairly and accurately designate space and allocate the corresponding cost between CIRM funded space and non-CIRM funded space. In fact, in the Application SDCRM had specifically designated 5,800 sf of the common space as associated with the non-CIRM funded space. The proposed adjustment to allocate 10,200 gsf of common space from the SDCRM space to the non-CIRM funded space and the corresponding $2.5 million reduction of the CIRM funded portion of the project does not consider the amount of this space that SDCRM had designated as non-CIRM funded space. Moreover, the method that CIRM staff used to allocate space (ratio of laboratory space) does not result in an accurate distribution of these spaces between the CIRM fund and non-CIRM funded spaces.

Contingency
On page 3 the Analysis notes that,

> *"The project budget includes $12.6 million or 15% of the estimated construction cost as project contingency. For a new project like that proposed, the contingency should not exceed 7.5%. Consequently, the staff argues that the contingency should be halved."*

The project budget includes $8.8 million, not $12.6 million, as a contingency. We believe that the amount of this contingency is reasonable in the circumstances.

Hensel Phelps Construction Company (HPCC) the contractor member of the SDCRM Facility development team has substantial relevant construction and estimating experience. HPCC prepared the estimate using schematic drawings in a cost model. Given the many remaining unknowns, the complexities of this project and HPCC's experience a 15% contingency reserve is not unusual and should not be considered excessive.

> Afterward, however, the Analysis indicates that *"the overall cost is lower than all other proposals in this category which raises concerns that some elements of the project may be under-budgeted and may not be fully operational at project completion."*

We see inconsistency between the suggestion that the contingency is too high and the simultaneously expressed concern that the overall cost is lower than other proposals. The Contingency cannot be considered separately from the building. Over time, the entire Contingency will be transferred or otherwise used to cover variances in other specific line items of the construction budget.

Given the stage of this project's development, experience informs us that certain items of cost may have been missed in the budget estimate and that some elements of the project may be under-budgeted. If the cost of items (such as those identified by staff as omitted from the current estimate) are transferred from the contingency to the Construction Budget as the design evolves from schematic to construction documents, the amount of contingency relative to the construction budget will more closely reflect the staff estimate.

While SDCRM has not studied other proposals carefully, possible explanations for SDCRM lower cost may be explained by, among other things SDCRM's building efficiency and the clean building site.

The ratio of net: gross square feet (building efficiency) of the SDCRM is 70%, or more than 10% higher than typical laboratory buildings. This design efficiency results in savings realized from having to build a 17,000 square foot *smaller* building shell and the corresponding conditioned space improvements. We estimate the value of the enhanced efficiency to be nearly $7 million or $70/gsf.

Moreover, the SDCRM site is a 'clean' building site that will require only modest site improvements and require no extraordinary staging costs.

Finally, we are confident given the considerable experience and expertise of the SDCRM development team that the construction budget combined with the 15% contingency is sufficient to complete the project and that concerns that elements of the project may not be fully operational at project completion are unwarranted.

Group 2 Equipment
On page 4, the Analysis notes,

> *"The [group 2 equipment budget] is substantially higher than other projects." The analysis indicates that a modular laboratory bench system will be employed with piped gases and utilities distributed within hollow portions of the laboratory furniture rather than within the building walls or ceilings."*

The Analysis recognizes that the higher equipment cost is attributable to the new organization with no existing equipment that can be relocated to the Facility. Moreover, the Facility includes substantial core facility equipment.

However, the comment about the benefits of modular equipment appears to be incorrect. While SDCRM does intend to use modular laboratory furniture, and the cost of this equipment is included in

the construction budget, such furniture does not obviate the construction of gas and other distribution systems as part of the Facility's tenant improvement.

Sustainability and Innovation
On page 5, the Analysis states,

> *"The application indicates that the design is expected to achieve a LEEDS certification at the silver level."*

This is incorrect. Sustainability is a vital interest of SDCRM. Consequently, the SDCRM facility expects to earn a Gold LEED certification.

Shared Facilities
On page 7 the Analysis suggests that,

> *"It is not clear, however, how these sharing opportunities will reduce the cost to CIRM for funded research grants."*

To clarify, SDCRM's considerable investment in Shared Facilities is intended to lower the cost to establish, operate and maintain, afford broad access, and ensure high quality output of these expensive technologies.

SDCRM's decision to establish shared facilities will reduce redundancies of equipment and expertise to deliver value to CIRM and all other providers of research funding. Concentrating equipment and expertise in shared facilities lowers the cost to establish, operate and maintain these expensive facilities, measurably increases the quality of the technology offering, improves the data and information produced, and helps to recruit and retain faculty.

The shared facilities that will be located at the SDCRM facility will be part of an extensive network of technology 'cores' located throughout the Torrey Pines Mesa at each of the four SDCRM member organizations or at any of its other academic or industrial collaborators.

SDCRM will only establish shared facilities in the Facility that must be located very close to the scientists and their experiments (animal imaging), or that do not exist in the network. Owing to extraordinary spatial or environmental requirements for which substantial investment elsewhere has already been made, engineering, large animal facilities, clinical care centers and GMP facilities could not be reasonably or cost effectively established in the Facility.

Conclusion
A $50 million investment in SDCRM is an efficient and effective use of taxpayer funds, delivering extraordinary value to California taxpayers. First, four highly respected organizations with excellent track records have allied to build one shared facility, instead of applying for as many as four separate facilities. An investment in SDCRM increases stem cell research capacity without wasteful redundancy.

The Facility is the most economical means to satisfy SDCRM's needs. The cost per square foot to construct the Facility is less than would be spent to lease a similarly equipped, but less prominently and proximally located, building.

The purpose-built Facility's spectacular location is nearly equidistant from each of the SDCRM member organizations amidst the large, thriving and interactive community of research institutes, biotechnology and pharmaceutical companies on Torrey Pines science mesa. The Facility provides the best means to engage SDCRM's members as well as the entire Torrey Pines science community to grow and support the collaborative, interdisciplinary science that is the foundation of a comprehensive CIRM Institute.

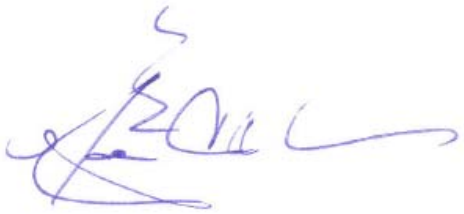
The Facility will meet the US Green Building Council's LEED (Leadership in Energy and Environmental Design) standard for **Gold** certification, not silver.

All of the foregoing notwithstanding, ultimately the value derived from and the true measure of the return on the California taxpayer's investment in CIRM funded facilities will be determined and delivered by ***scientific productivity*** enabled and enhanced by those investments.

Scientific productivity is enabled by the quantity, and determined by quality of the science. The SDCRM resident and non-resident faculty members are leading researchers with outstanding track records for obtaining research funding and publishing influential peer-reviewed papers. SDCRM member scientists have been awarded $60 million or 23% of all grant funds awarded by CIRM to date and have published many papers reporting new insights into basic and translational stem cell biology. As successful as they have been, we expect that the Facility will make SDCRM scientists even more competitive for substantial future research funding from CIRM and other sources. If so, California taxpayers can be assured that SDCRM will not just use this shared facility for stem cell research for at least 10 years, as is required, but will do so *productively*.

The Facility will be a focal point for stem cell science that will catalyze increased collaboration among the stem cell research community. CIRM's investment in the SDCRM facility will create an environment of excellence that will ensure that future government dollars are put to work most efficiently via team-driven science.

Very truly yours,



Louis R. Coffman
Vice President

Cc: Edward W. Holmes, MD, President & Chief Executive Officer